A Design of Experiment Approach to Predict Process and Product Parameters for a Spray Dried Influenza Vaccine

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PURPOSE

Introduction
Liquid vaccines need to be stored at 2-8 °C. Dependency on cold chain makes distribution of liquid vaccines complex and expensive that could potentially be overcome by using dried powder vaccines. Spray drying (SD) is an established method for drying pharmaceutical biologicals. Drying liquid vaccines by SD method can produce powders with desired physiochemical and morphological properties (fig 1).

The issue
Spray drying process for experimental vaccines are mostly optimized by one-factor-at-a-time (OFAT approach), that has several disadvantages (fig 2). In contrast to OFAT, Design of Experiments (DoE) is a structured approach to identify critical and non-critical parameters for production and this approach can be applied to produce dry powder vaccines.

The goal
Therefore, the objective of this study was to investigate the use of a Design of Experiment (DoE) approach to systematically screen and optimize the spray drying process variables and predicting product quality parameters for dried powder vaccine.

METHOD

Whole inactivated influenza virus (WIV) vaccine was used as the model vaccine with Trehalose (100-150 mg/mL) as stabilizing excipient. The process parameters investigated were inlet air temperature (110-160 °C), nozzle gas flow rate (7.3-17.5 L/min) and feed flow rate (1.0, 3.4 and 4.5 mL/min). The WIV vaccine powder (product parameters) investigated were particle size, residual moisture content, powder yield and Antigenicity. Spray drying experiments were performed based on the Central Composite Family (CCF) design consisting of 23 experimental runs. Results obtained from vaccine powder analysis were analyzed with software MODDE 10.0 and the relation between different parameters was studied.

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RESULTS

Vaccine powders with a broad range of physical characteristics (RMC 1.2 - 4.9 %, particle size 2.4 - 8.5 µm and powder yield 42.82 %) were obtained. WIV showed no significant loss in antigenicity.

Furthermore, descriptive models (fig 3 and 4) generated by DoE could be used to predict process settings (inlet air temperature, nozzle gas flow rate, feed flow rate and excipient concentration), that subsequently could be used (set) to generate a dried WIV powder with predefined (predicted) characteristics (fig 5). Moreover, the spray dried vaccine powders retained their antigenic stability even after storage for 3 months at 60 °C.

CONCLUSION

The current study successfully demonstrates the application of QbD principles and the DoE approach in the development of a dry powder influenza vaccine formulation. The WIV vaccine powder was thermostable that could be potentially used for pulmonary administration.